

Cestode Infections of Mammary Glands and Female Reproductive Organs: Potential for Vertical Transmission?

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ABSTRACT: A widely studied aberrant strain of tetrathyridia of *Mesocostoides vogei* infecting laboratory mice is the only cestode for which vertical transmission has been verified experimentally. Vertical transmission has been reported for *Taenia saginata* in cattle and *Echinococcus* sp. in humans, but the validity of these cases has proved difficult to verify. However, metacestode stages of *Taenia solium*, *Echinococcus granulosus*, *Echinococcus multilocularis*, *Multiceps* sp., *Diphyllobothrium mansonii*, *Spirometra erinacei*, and *Proteocephalus ambloplitis* have been reported from the mammary glands, uterus, placenta, and/or ovary of several naturally infected hosts. Such infection foci, particularly the mammary glands, suggest a potential for vertical transmission in these species. Such possibilities warrant further study in these and other cestodes. Field surveys of hosts should be conducted to elucidate the prevalence of cestode localization in female organs in which there is potential for transmission.

KEY WORDS: Cestoda, *Echinococcus*, mammary glands, maternal transmission, *Mesocostoides*, placenta, pre-natal, sparganosis, *Taenia*, uterus.

In recent years, interest in vertical transmission of parasitic organisms has grown substantially. This has resulted in the elucidation of several fascinating examples of transmammary and intrauterine transmission of parasites as reviewed by Shoop (1991). Increased research activity over the past 2 decades has revealed that vertical transmission is common among many nematodes and trematodes. Conversely, the limited data available seem to suggest that vertical transmission is not common among cestodes. However, efforts to identify cases of vertical transmission among cestodes have been fewer than those involving nematodes and trematodes. Many cestodes have been reported to localize in female organs, which suggests the potential for vertical transmission. The present review summarizes the published cases of vertical transmission and invasion of female organs by cestodes and suggests directions for future research in this area.

The Concept of Vertical Transmission

In this review, vertical transmission is defined as the transmission of parasites directly (i.e., without any intervening period either outside a host or in a host of another species) from a living parent (usually a mother) to its viable offspring in which parasite reproduction can occur. This may occur in parasites having either monoxenous or heteroxenous life cycles and restricts the concept of vertical transmission to those situations involving specific parental/filial relationships.

Living parent condition

By including only living parents, transmission by cannibalism as proposed by Mead and Olsen (1971) for *Ophiotaenia filaroides* plerocercoids and by Kroeze and Freeman (1982) for *Taenia crassiceps* cysticerci can be eliminated. As these authors suggested, cannibalism may have important epizootiological implications. However, cannibalism may occur among siblings and frequently involves a parent eating its young rather than vice versa. Thus, it is more accurate to regard this as a type of paratenesis that happens to involve intra- rather than interspecific exchange.

Reproduction in offspring condition

The inclusion in the preceding definition of only parasites having the potential to reproduce within the filial host ensures that the only cases recognized are those in which transmission results in the establishment of a new source of parasite dissemination. This epizootologically relevant condition excludes those cases in which microfilariae are transmitted transplacentally to unborn young as has been described for several species of filarial nematodes (Eberhard et al., 1993). Transplacental transmission of microfilariae obviously involves a specific parental/filial relationship but does not actually result in permanent establishment of parasites in the young. The only epizootiological significance of this would be the chance that the total number of reservoirs available to insect vectors would be increased temporarily. However, even this may

be unimportant inasmuch as the intensity of congenital microfilaremia in most cases is probably so low that the potential for transmission to insect intermediate hosts is negligible (Mantovani and Jackson, 1966).

Vertical transmission of helminths has been demonstrated conclusively only among placental mammals. In the case of prenatal transmission this is not surprising given the lack of transmission routes available in oviparous hosts. Among insect hosts, Fay (1961) stated that some evidence existed for occasional passage of *Leidy-nema appendiculata* eggs within the oothecae of cockroaches, though she presented no data. Among avian hosts, trematodes of the genus *Prosthogonimus* inhabit the oviducts and occasionally the shelled eggs (Schell, 1985) but have not been reported to invade the developing chicks. All known cases of postnatal vertical transmission of helminths involve transmammmary passage of the helminth into the nursing young. However, postnatal vertical transmission of protozoan symbionts is known to occur among termites during trophallaxis and proctodeal feeding (Cleveland, 1928). There may be some potential for postnatal vertical transmission among esophageal nematodes of birds that feed their young by regurgitation from the crop. Potential candidates for further study of this possibility might include parasites such as species of *Capillaria* that are capable of autoinfection of their avian hosts. In such cases, both paternal and maternal relationships might be involved.

Vertical Transmission of Cestodes

All helminths that are known to undergo vertical transmission are characterized by a histozoic migratory stage in the life cycle. Such a migratory habit possibly provided an essential preadaptation for those species that penetrate the placenta, uterine wall, or mammary glands. Considering this, it is not surprising that most vertically transmitted helminths are nematodes, particularly strongylates and ascaridoids (Miller, 1981; Lyons, 1994) or strigeoid trematodes (Shoop, 1991, 1994).

Vertical transmission appears to be rare among cestodes in comparison with nematodes and trematodes. This may be related to the fact that virtually all adult tapeworms inhabit the intestinal lumen of their vertebrate hosts. This is also true of adult strigeoids, strongylates, and ascarids, but the juveniles of these nematodes gen-

erally undergo more extensive histozoic migration than do the larvae and juveniles of cestodes. The only histozoic migratory stages of cestodes are the oncospheres and, in some species, the metacestodes. In most cestode taxa, these stages are restricted to oviparous arthropod intermediate hosts where, as discussed above, vertical transmission is unlikely. Notable exceptions to this include the pseudophyllideans, the proteocephalideans, and the cyclophyllidean families Taeniidae and Mesocestoididae. Each of these groups has oncospheres and/or metacestodes that migrate through the tissues of vertebrate intermediate hosts, so it is not surprising that some species of each group have been reported to infect mammary glands or female reproductive organs (Table 1).

Taeniids have received more attention than other cestodes, probably because of their veterinary and medical importance. Vertical transmission of taeniids would be possible only at the oncosphere or metacestode stages. If it occurred, transmission of oncospheres could result in cysticercosis, coenurosis, or hydatidosis (depending on the taeniid species) in the young of infected mothers. *Taenia solium* might present an interesting case because humans can serve as both intermediate and definitive host, thereby resulting in either cysticercosis or adult taeniasis in the young of infected mothers.

Shillinger and Cram (1923) cited several authors whose early reports of congenital *E. granulosus* hydatidosis in humans were thought to have been misdiagnoses of nonparasite fetal anomalies. Shillinger and Cram's (1923) opinion was cited in a more recent review by Loke (1983), who neither agreed nor disagreed with their interpretation. Similarly, Gluhovschi et al. (1970) reported the occurrence of 6 large but "sterile" hydatid cysts of *Echinococcus granulosus* in the viscera of an unborn calf whose mother had an abnormal placenta. The authors regarded this as a rare instance of prenatal hydatidosis in which transmission of oncospheres had been facilitated by placental pathology. However, although the cysts looked like hydatids upon gross examination, the fact that they were "incompletely developed" and "sterile" made absolute identification impossible.

Several authors have reported evidence for prenatal transmission of *Taenia saginata* (= *Cysticercus bovis*) among cattle. McManus (1960) reported a 3.07% prevalence of cysticercosis bovis among 14,855 Kenyan calves, some of which

Table 1. Cestode infections reported from female organs. All are metacestodes except where noted.

Cestode species	Mammary	Uterus	Placenta	Ovary	References*
Cyclophyllidae: Mesocestoididae					
<i>Mesocestoides vogei</i>	Mouse	Mouse	Mouse		7, 11, 23
Cyclophyllidae: Taeniidae					
<i>Echinococcus granulosus</i>	Human	Human		Human	3, 10, 15
<i>Echinococcus multilocularis</i>		Human			18
<i>Echinococcus</i> sp.	Human	Human		Human	2, 4, 8, 9, 16, 19, 20
<i>Multiceps</i> sp.	Human				12
<i>Taenia crassiceps</i>	Mouse				6
<i>Taenia solium</i>	Human				1, 13, 21, 22
<i>Taenia</i> sp. (gravid proglottid)		Human			17
Proteocephalidae: Proteocephalidae					
<i>Proteocephalus ambloplitis</i>				Bass	14
Pseudophyllidae: Diphyllbothriidae					
<i>Diphyllbothrium mansonii</i>	Human				5
<i>Spirometra erinacei</i>	Human				24

* References: 1 = Alagaratnam et al., 1988; 2 = Alvarez et al., 1985; 3 = Atasü et al., 1988; 4 = Chiva et al., 1987; 5 = Chuen-Fung and Alagaratnam, 1991; 6 = Conn, present report; 7 = Conn and Etges, 1983; 8 = Epstein, 1969; 9 = Gaspa and Eusebi, 1973; 10 = Georgakopoulos et al., 1980; 11 = Hess, 1972; 12 = Kurtysz et al., 1983; 13 = Leggett, 1983; 14 = McCormick and Stokes, 1982; 15 = Ouedraogo, 1985; 16 = Prokopenko, 1989; 17 = Schacher and Hajj, 1970; 18 = Semchyshyn, 1974; 19 = Thurairatnam, 1992; 20 = Turan and Küçükorgulu, 1987; 21 = Viratchai and Jimakorn, 1981; 22 = Vuong, 1989; 23 = Williams and Conn, 1985; 24 = Yamane et al., 1975.

were as young as 2 days postpartum. Urquhart (1961) reported bovine cysticercosis in 18 young Kenyan calves; it was his opinion that only 1 of these was acquired prenatally, the others being acquired shortly after birth. Haas (1967) speculated that generalized cysticercosis in a 3-wk-old calf was acquired prenatally. Šlais and Mann (1976) reported cysticerci of *T. saginata* from 2 calves in Kenya; the calves were 21 and 27 days old when necropsied, but the scolex anlagen of the cysticerci conformed morphologically to stages that develop only after 4–6 mo. Each of these authors concluded that the infections occurred prenatally. However, because no experimental infections were involved these reports do not constitute definitive proof of prenatal transmission.

Some attempts have been made to verify experimentally the occurrence of prenatal transmission of taeniid cestodes. No infections were found among calves born to 8 pregnant cows that had been exposed experimentally to 500–150,000 eggs of *T. saginata* by Urquhart (1961). In a similar experimental study, Kozakiewicz (1975) infected 15 cows with cysticerci of *T. saginata* by exposing them to 500,000 eggs each; the cows ranged from 5 to 8 mo of pregnancy at the time of exposure. When euthanized and necropsied

within 10–14 days postpartum, their calves lacked cysticerci.

The only experimentally verified cases of vertical transmission of cestodes have involved laboratory rodents infected with the aberrant tetrathyridia of *Mesocestoides vogei* (= *Mesocestoides corti* of Specht and Voge, 1965). Eckert (1970) was the first to report tetrathyridia in very young rats but gave no direct evidence of vertical transmission. Definitive experimental work was done by Hess (1972), who provided strong evidence for transmammary transmission of tetrathyridia in mice but expressed uncertainty as to whether the worms entered the milk ducts or migrated directly through the teats. Hess (1972) further provided equivocal evidence for in utero transmission but failed to use adequate controls to eliminate the possibility of transmammary transmission immediately postpartum. These results were summarized by Baer (1972), Miller (1981), and Stoye (1976) in reviews of milk-borne transmission of helminths.

Because of the uncertainties of earlier studies, Conn and Etges (1983) performed a detailed set of experiments using prenatal and early postnatal examinations of mice from mothers infected experimentally with tetrathyridia; they also used reciprocal cross-fostering techniques with neo-

nates of infected and uninfected mothers. The resulting data from 132 fetuses and 32 neonates showed no evidence of prenatal transmission, although a few tetrathyridia did penetrate into the uterine lumen and 1 was found in the maternal portion of a placenta. Conversely, the data conclusively demonstrated a 62% rate of transmammary transmission. Besides clarifying the basic mode of vertical transmission of this species, Conn and Etges (1983) showed that tetrathyridia entered the milk ducts of the mother mice, thus becoming positioned for immediate transmission to the young at the first nursing event. In a follow-up study, Williams and Conn (1985) provided some data on mammary gland histopathology associated with infection by tetrathyridia. They also presented quantitative data on the distribution of tetrathyridia within the mammary gland fat pads; these data suggested that the parasites did not localize preferentially in the mammary tissue but probably occurred there as a result of subcutaneous migration related to other unknown factors. Thus, it appears that transmammary transmission in this species is fortuitous. This is quite unlike the highly regulated vertical transmission of many nematode and trematode species (Shoop, 1991).

Cestodiasis of Mammary Glands and Female Reproductive Organs

Despite the few confirmed cases of vertical transmission among cestodes, there are numerous reports of cestodes occurring in female organs from which such transmission might be possible (Table 1). All but 1 of these cases involved metacestode stages. The single exception was a gravid proglottid of *Taenia* sp. that apparently had crawled from the anal area through the vagina and into the uterus of a woman (Schacher and Hajj, 1970).

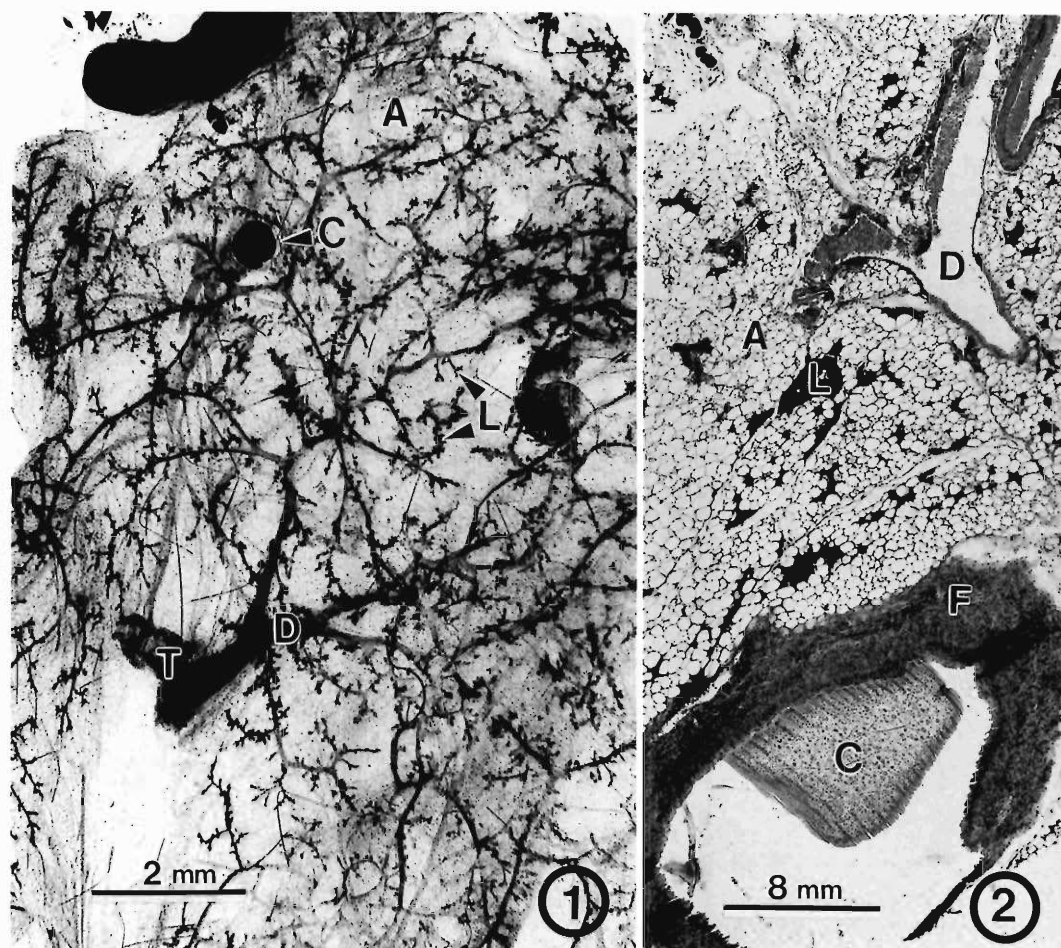
Table 1 shows that most of the reports of metacestodes occurring in female organs have resulted from experimental infections of laboratory mice or clinical cases of human infections. Most of the latter have involved the mammary glands, where cysticerci, hydatid cysts, and plerocercoids (spargana) have been encountered during routine cancer-screening examinations for breast lumps. Uterine cestodiasis have been discovered primarily during obstetrical or gynecological examinations. Inasmuch as these cestodiasis were reported because of their clinical significance to individual patients, estimates of the prevalence

of such infections among women based on a survey of the literature undoubtedly would underestimate the true prevalence. Even among humans, the host species most studied in this respect, it is likely that subclinical cases of mammary, uterine, placental, or ovarian cestodiasis are quite common. This seems particularly likely when one considers that the vast majority of human cestodiasis occur in areas of the world where mammograms and modern obstetrical examination tools are not readily available or affordable.

Other than the case reports cited above, few studies have examined the clinical consequences of cestodiasis of female organs. Williams and Conn (1985) described the histopathology of mouse mammary glands infected by tetrathyridia of *M. corti*. They reported host responses that increased in severity as parasite density increased; responses ranged from localized inflammation with little or no loss of lactogenic tissue, to generalized fibrous hyperplasia resulting in complete destruction of lactogenic tissue. Among human patients, occasional reports have described the co-occurrence of hydatid cysts and mammary carcinomas in women (Gaspa and Eusebi, 1973; Alvarez et al., 1985). However, no study has demonstrated a causal relationship between the 2 conditions. Such situations are very rare and are noteworthy only because of the complications they cause in diagnosis of cancer. Schacher and Hajj (1970) reported an isolated case of postmenopausal bleeding associated with the presence of a proglottid of *Taenia* sp. in the uterus of 1 woman. Hydatid cysts in the uterine wall and around the uterus during pregnancy have been reported to cause difficulties in labor among women (Semchyshyn, 1974).

Directions for Future Research

The fact that few cestodes have been reported to employ vertical transmission in their life cycles does not necessarily mean that such transmission is rare. Vertical transmission among other helminth and protozoan parasites was overlooked for many decades and is difficult to demonstrate in most cases (Miller, 1981; Shoop, 1991). Likewise, the rarity of reports of cestode infestations of female organs does not necessarily imply that cestodes do not frequently invade those organs. Conversely, it is possible that many cestode species invade the mammary glands of their hosts. Such cases may be reported simply (and



Figures 1, 2. Brightfield light micrographs showing cysticerci of *Taenia crassiceps* (KBS strain) in the mammary glands of laboratory mice experimentally infected by intraperitoneal inoculation. 1. Whole mount of a pressed posterior mammary gland stained with Semichon's acetocarmine. An encapsulated cysticercus (C) is present among the lactogenic alveoli (L) that branch throughout the adipose tissue (A) of the fat pad. The teat (T) and lactiferous ducts (D) are clearly discernible. 2. Histological section (10 μ m thick) showing a cysticercus (C) within a host-derived fibroblastic capsule (F) within a posterior mammary gland. The adipose tissue (A), lactiferous ducts (D), and lactogenic alveoli (L) appear unaffected by the presence of the encapsulated worm.

ambiguously) as involving subcutaneous foci, when in fact the mammary glands, because of their location and configuration, are almost certainly included in many such examinations. Most reports of parasite surveys do not mention subcutaneous examinations, so mammary glands and other subcutaneous foci are probably underreported as sites of parasite localization. Based on this paucity of information, the following 2 suggestions for future research hold promise for uncovering cases of vertical transmission among cestodes.

First, future parasite surveys of mammalian

hosts should incorporate examination of mammary glands as a routine part of their protocols. Many taeniid and diphyllbothriid metacestodes are known to occur commonly or even predominantly in subcutaneous regions near mammary tissues (Delvalle, 1989; Whittington et al., 1992; Keeling et al., 1993). Additionally, studies should be initiated with the primary focus of searching for mammary helminthiasis in natural host populations. This has not been done for any group of helminths, including cestodes. A good starting place would be to look at small rodents whose mammary glands can be removed in toto and

processed as whole mounts such as those prepared by Conn and Etges (1983) and Williams and Conn (1985). Such whole mounts allow not only relatively rapid screening for mammary helminths but also determination of specific locations of the helminths in relation to lactiferous ducts, lactogenic alveoli, and other organ components. Additional information on basic host responses to the parasites can be obtained if half the mammary glands from each host are mounted whole for rapid screening, while half are prepared for routine histology. Examples of these complementary techniques are shown from experimental infections of *Taenia crassiceps* in mouse mammary glands in Figures 1 and 2. Searching for the presence of cestodes in mammary glands of larger mammals might be accomplished using enzymatic digestion of excised glands. This technique would not give as much information as the former but would at least allow an assessment of the prevalence of mammary helminthiasis among larger host species.

Second, some research should be focussed on experimental work with individual cestode species that seem particularly well suited for vertical transmission. The best candidates would be the species listed in Table 1, or any other species with oncospheres and/or metacestodes that undergo histozoic migration in mammalian hosts. *Taenia crassiceps* might provide an ideal experimental model because it can live in laboratory rodents. Also, *T. crassiceps* undergoes histozoic migration in both oncosphere (Freeman, 1962) and cysticercus (Kroeze and Freeman, 1982, 1983) stages. Furthermore, this species localizes preferentially in subcutaneous sites, many of which are near mammary glands (Freeman, 1962; Delvalle, 1989). This species also has the advantage of undergoing asexual proliferation in the cysticercus stage; this would result in more rapid buildup and, thus, easier detection in newly infected fetal or newborn hosts.

In conclusion, metacestode stages of cestodes frequently occur in female organs of mammalian hosts where there is a distinct potential for vertical transmission. Few cases of vertical transmission have been demonstrated conclusively, but little research effort has been made in this area (Mackiewicz, 1988). Recently, increased awareness of the epizootiological importance of vertical transmission among some nematodes and trematodes should encourage more rigorous searching for evidence of this phenomenon among cestodes.

Acknowledgments

I am grateful to Herbert Haines and Michael Sukhdeo for their work in organizing the symposium for which this review was prepared. I also thank the New Jersey Society for Parasitology for providing funding that helped with the presentation of this work. I am grateful to James R. Coggins for providing me with the stock of *Taenia crassiceps* used herein.

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